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NEUROLEPTIC USE IN THE TREATMENT OF POST-TRAUMATIC STRESS DISORDER

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Background. There have been few studies of the use of neuroleptics in the treatment of Post-Traumatic Stress Disorder (PTSD). This study uses data from two large outcome studies to: (1) examine demographic and treatment characteristics associated with neuroleptic prescription in the treatment of PTSD, and (2) compare the outcomes of neuroleptic-treated patients with those not receiving neuroleptics. *Methods.* A secondary analysis of an observational outcome study of 831 inpatients and 554 outpatients (all males) receiving treatment at the VA for combat-related PTSD was performed. Patients were classified as having either received neuroleptics during the following year or not. Sociodemographic characteristics, treatment and medication history and detailed information about PTSD symptoms were obtained at baseline and 12 months. First, the two groups were compared with respect to the demographic and

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clinical variables. We then conducted a series of separate paired t-tests to determine whether there was significant improvement from baseline to follow up in each group and a series of analyses of covariance that compared outcomes in the two groups, adjusting for baseline differences. *Results.* Approximately 9% of inpatients and 10% of outpatients were treated with neuroleptics. Patients who received neuroleptics had both more psychiatric and more social impairment. They also demonstrated more severe PTSD (especially intrusive symptoms) despite having similar combat exposure. Outcomes after one year for the group treated with neuroleptics were not significantly different from the group not treated with neuroleptics. *Conclusions.* Neuroleptic use in the treatment of PTSD is targeted at more seriously ill patients and was not associated with substantial improvement.

KEY WORDS: PTSD; neuroleptics; treatment; outcome.

INTRODUCTION

Combat-related Post-Traumatic Stress Disorder (PTSD) is frequently a persistent and severe mental illness, with half of the Vietnam veterans who exhibited full PTSD symptoms at some time after the war still fulfilling criteria over 20 years later (1). The Department of Veterans Affairs (VA) first began establishing distinct inpatient and outpatient programs for the treatment of PTSD in the late 1970's.

While concerns have been raised that despite this dedication of resources, the development of successful psychopharmacologic treatment strategies has been slow (2), there have been some notable advances in the use of medications in combat-related PTSD. Treatment with the selective serotonin re-uptake blocker fluoxetine has been shown to reduce the numbing and arousal symptoms associated with PTSD (3). Several studies have reported that the monoamine oxidase inhibitor phenelzine produced moderate to good improvement in the majority of patients, primarily through reduction in re-experiencing symptoms and insomnia; avoidant/numbing, hyperarousal, depressive and anxiety/panic symptoms did not improve (4).

One of the hallmark symptoms of PTSD is the often extremely vivid "reliving" of traumatic experiences. It has been reported that at least one third of inpatients (5) and nearly one half of outpatients (6) seeking treatment for combat-related PTSD report auditory hallucinations with at least some guilt or combat themes. While these symptoms are not associated with schizophrenia-spectrum diagnoses, the presence of major depression has been observed significantly more often in outpatients with PTSD and psychosis than in the non-psychotic veterans (5). The

use of antipsychotic medication may thus be indicated in the treatment of these particularly distressing psychotic symptoms observed in a large fraction of patients with combat-related forms of PTSD (7).

There have been few studies of the use of neuroleptics in the treatment of PTSD. In the most complete review of medication prescribing practices in PTSD among inpatients (8), it was demonstrated that, of patients treated with any medication, 26% received neuroleptics, and three of the four most prescribed combinations of medications included neuroleptics. It also does not appear that the degree of neuroleptic usage observed is simply explained by treatment of co-morbid psychotic disorder in patients with PTSD, since, in the same study, only 2% had a concurrent diagnosis of schizophrenia or schizoaffective disorder. Even when other diagnoses that might be treated with neuroleptics (e.g. bipolar and depressive disorder) are included, this only represents approximately 12% of the veterans in the study. Other reports of rates of comorbid schizophrenia range from 0% (although over one third of the group endorsed psychotic items) (9) to 7% (10).

There are no reports of randomly assigned, controlled trials of the use of neuroleptics in the treatment of PTSD, although there have been several reports of their use. There is no consensus in the literature on the value of neuroleptic treatment of PTSD. There have been reports of neuroleptic treatment failing to ameliorate PTSD-related auditory hallucinations (11) or PTSD symptoms overall (12), as well as improving both PTSD and psychotic symptoms (13–15).

None of the previous studies used data from large systematically evaluated patient samples. In contrast to these prior efforts, the current study uses data from two large outcome studies to examine demographic and treatment characteristics associated with neuroleptic prescription in the treatment of PTSD and to compare the 12-month outcomes of neuroleptic-treated patients with those not receiving neuroleptics.

METHODS

Subjects

Data for this secondary analysis were derived from two studies of the outcome of inpatient and outpatient treatment of male veterans with combat-related PTSD in the VA. Detailed descriptions of these studies and the treatments provided are provided elsewhere (16,17). In the first study, outpatients ($n = 554$) enrolled from 1990 to 1991 were treated by 6 specialized PTSD treatment teams and followed for one year. In the

second study, inpatients ($n = 831$) enrolled from November 1991 until January 1994 were treated on 10 different inpatient treatment units and also followed for one year.

Neuroleptic exposure was established at baseline 4, 8, and 12 months through medication review. Patients were classified to one of two groups: (1) patients who were never prescribed neuroleptics during the course of their one year in the study (noNL) and, (2) patients who received neuroleptics at one or more time point during the year (NL).

Data Collection

The data were collected by trained research assistants performing face-to-face interviews with the veterans at the various sites. At the time of enrollment into the study, informed consent was obtained and an extensive baseline assessment addressing socio-demographic characteristics and health status (including substance abuse) was performed. Follow-up interviews were completed at 4, 8, and 12 months.

Measures

Admission clinical psychiatric diagnoses were based on DSM-III-R criteria. Alcohol, drug, and psychiatric problems were assessed by using composite indices from the Addiction Severity Index (ASI) (18). General psychological distress and distress due to psychotic symptoms were assessed with the global severity and psychoticism indices, respectively, of the Brief Symptom Inventory (BSI) (19). Post-traumatic stress disorder symptoms were assessed using the Mississippi Scale for Combat-Related Post-Traumatic Stress Disorder (20). Combat exposure was assessed using the Legacies Combat Scale (21). VA compensation status for PTSD and/or other psychiatric conditions was recorded as a percentage from 0 to 100%.

Hallucinations, violent behavior, serious suicidal thoughts and/or attempts were assessed with dichotomous measures from the ASI. Service utilization, including lifetime hospitalization for PTSD and other psychiatric disorders and exposure to specific medication classes, was also obtained from patient interviews. Employment was assessed by the number of days worked and the amount of money earned in the 30 days prior to evaluation.

Data Analysis

Patients with diagnoses of schizophrenia or schizoaffective disorder were excluded since neuroleptic treatment of these disorders would

confound examination of the impact on the treatment of PTSD. All subjects without a diagnosis of PTSD were also excluded. A total of 405 (81%) outpatients and 782 (94%) inpatients met these inclusion criteria. Inpatients and outpatients were analyzed separately as it was thought that combining these two treatment groups might obscure significant treatment effects.

The initial analysis consisted of *t*-tests and chi square tests comparing the two groups with respect to demographic and clinical variables. A step-wise logistic regression was then performed to identify a smaller subset of variables that captured differences between the groups. We then conducted a series of separate paired *t*-tests to determine whether there was significant improvement from baseline to follow up in each group. Next, we conducted a series of analyses of covariance (ANCOVAs) that compared outcomes in the two groups, adjusting for baseline differences between the groups. In these analyses the dependent variables were 12-month outcomes. Covariates included baseline values of the dependent variables and propensity scores (22)-a now well-accepted method for adjusting for group differences in non-experimental studies. Logistic regression was performed in which the dependent variable was a dichotomous indicator of neuroleptic exposure and the predictor variables were potential confounders of the treatment-outcome association identified for the inpatient and outpatient samples. From the fitted model, each subject's log odds (logit) of receiving neuroleptics was computed based on the linear combination of their respective sets of values for the predictors. The logit was then converted to its corresponding probability, and this value was used as the subject's 'propensity score', a measure of the multivariate similarity to the individuals treated with neuroleptics.

Analyses of 4 and 8-month outcomes failed to reveal any substantial differences from 12-month outcomes, and thus, only the 12-month outcomes are reported.

RESULTS

Results are presented for the inpatient sample first followed by the outpatient group.

Inpatients

Baseline Characteristics. Comparisons of demographic and treatment variables are presented in Table 1. There were several significant demographic differences between the two groups. The NL group ($n = 67$) was slightly younger, less likely to be white, more likely to be married,

TABLE 1
Baseline Characteristics of Veterans Treated in Specialized Inpatient PTSD Units

	Never Received ($n = 715$)		*Neuroleptic Exposed* ($n = 67$)		*Analysis*		
Characteristic	*Mean*	*SD*	*Mean*	*SD*	*T*	*df*	*p*
Veterans age	44.8	3.11	43.69	2.398	2.9991	62.3	0.0039
Legacies combat score	11.21	2.335	11.45	2.12	0.8131	780	ns
Mississippi scale total	134.4	16	140.3	13.94	2.8532	753	0.0044
Percent service conn for psych (incl PTSD)	27	1	58	30	4.7363	418	<.0001
Amount take home pay past 30 days	170.4	483.6	34.33	172.8	4.8915	189.2	0.0001
Ment hlth adm to VA	0.61	0.94	1.08	1.09	3.8024	779	0.0002
Clinical Symptoms: PTSD							
Mean SCID intrusion symptoms	1.724	0.401	1.851	0.282	3.3673	93	0.0011
Mean SCID numbing and avoidance symp	1.736	0.305	1.79	0.2719	1.4688	780	ns
Mean SCID hyperarousal symptoms	1.865	0.253	1.863	0.234	0.0558	780	ns
Mean SCID guilt symptoms	1.641	0.595	1.746	0.480	1.6862	86.3	ns
Mean SCID DSM-IIIR symptoms	1.774	0.238	1.835	0.207	2.0134	780	0.0444
Mean all SCID symptoms	1.707	0.357	1.79	0.289	2.2054	86.2	0.0301
Addiction Severity Index							
ASI alcohol composite	0.113	0.191	0.128	0.218	0.508	779	ns
ASI drug composite	0.033	0.081	0.045	0.093	1.1128	779	ns
ASI employment composite	0.574	0.221	0.614	0.209	1.4338	779	ns
ASI psychiatric composite	0.642	0.155	0.747	0.154	5.3163	780	<.0001

Brief Symptom Inventory							
BSI psychoticism subscale	2.432	0.7849	2.463	0.7043	0.3117	754	ns
BSI total	2.418	0.6873	2.467	0.7055	0.5452	754	ns
	N	%	*N*	%	χ^2	*df*	*p*
Marital status (married)	275	38.46	38	56.72	8.5	1	0.0035
Race (white)	547	76.5	39	58.21	10.92	1	0.00095
Service connected for PTSD	359	50.21	49	73.13	12.902	1	0.001
Service connected psych-other than PTSD	20	2.8	5	7.46	4.309	1	0.038
Working now?	107	14.97	3	4.48	5.57	1	0.018
Ever hosp for psychiatric diagnosis	493	68.95	59	88.06	10.77	1	0.001
Taking anxiolytic	171	23.92	40	59.7	39.818	1	0.001
Taking antidepressant	319	44.62	45	67.16	12.519	1	0.001
Experience hallucinations-past 30 days	140	19.58	26	38.81	13.541	1	0.001
Trouble violent behavior-past 30 days	284	39.78	40	59.7	10.018	1	0.002
Serious suicide thoughts-past 30 days	293	41.04	44	65.67	15.154	1	0.001
Attempted suicide-past 30 days	46	6.43	14	20.9	18.086	1	0.001

more often service connected for PTSD, and had higher disability ratings than the noNL group ($n = 715$). The NL group was also more likely to be rated as disabled by another psychiatric disorder to some extent, was significantly less likely to be working at the time of initial evaluation, and made less money.

There were also differences in the severity of PTSD symptoms. While there were no significant differences between the noNL and NL groups with respect to the combat scale score, veterans in the NL group had significantly higher Mississippi scale total scores and more intrusive ("reliving") PTSD symptoms. The two groups did not differ significantly in the number of numbing and avoidance, hyperarousal, or guilt symptoms. There were no significant differences in measures of alcohol or drug use or the severity of general psychological distress as measured by the BSI.

Differences in previous treatment and symptoms were also seen. Neuroleptic-treated veterans were significantly more likely to have been hospitalized in a psychiatric facility previously and to be taking concurrent anxiolytic or antidepressant medication. There were no significant differences in the rates of co-morbid alcohol abuse/dependence, drug abuse/dependence, affective, dissociative, bipolar, adjustment, or sleep disorders. The NL group was also significantly more likely to report having experienced hallucinations and trouble with violent behavior in the 30 days prior to enrollment. A significantly greater number of these veterans reported experiencing serious suicidal thoughts and having attempted suicide over this same time period.

Logistic regression demonstrated that several variables independently predicted receipt of neuroleptics: age ($p < 0.025$), admissions to VA psychiatric hospitals ($p < 0.017$), ASI psychiatric composite at intake ($p < 0.022$), race ($p = 0.004$), service connection for PTSD ($p < 0.034$), "ever hospitalized for a psychiatric problem" ($p = 0.0032$), and taking anxiolytic medication ($p = 0.0001$).

Outcomes. At 12 months (Table 2), the NL group demonstrated significant improvement in psychiatric problems on the ASI. Paradoxically, there was also significant worsening of the index of general subjective distress as well as the psychotic subscale of the BSI. There were no significant changes in severity of PTSD symptoms, measures of alcohol or drug use, or employment.

The noNL group demonstrated a significant increase in PTSD symptoms and distress on the general severity index and psychotic subscale of the BSI. There was, however, a significant decrease in the number of total psychiatric symptoms. There were also no significant changes in employment and drug or alcohol use in the noNL group.

TABLE 2
Twelve Month Outcomes for Veterans Treated in Specialized Inpatient PTSD Units

	n	*Baseline*	*SD*	*1 Year*	*SD*	*t*	*p*
Mississippi Total Score							
noNL	396	135.318	15.321	137.152	17.476	2.378	0.0179
NL	44	141.102	13.899	140.045	18.747	0.498	ns
ASI Psychiatric Composite							
noNL	462	0.641	0.161	0.59	0.18	5.729	0.0001
NL	53	0.759	0.155	0.672	0.169	3.241	0.0021
ASI Alcohol Composite							
noNL	462	0.104	0.181	0.103	0.16	0.076	ns
NL	53	0.133	0.232	0.123	0.211	0.272	ns
ASI Drug Composite							
noNL	462	0.03	0.075	0.03	0.078	0.032	ns
NL	53	0.043	0.089	0.061	0.132	1.427	ns
ASI Employment Composite							
noNL	462	0.557	0.211	0.544	0.204	1.194	ns
NL	53	0.597	0.196	0.589	0.2	0.287	ns
BSI Psychoticism							
noNL	396	2.424	0.761	2.546	0.814	2.841	0.0047
NL	45	2.459	0.716	2.707	0.939	2.04	0.0474
BSI Total Score							
noNL	396	2.448	0.674	2.599	0.692	4.426	0.0001
NL	45	2.472	0.668	2.711	0.768	2.231	0.0308

After adjusting for the propensity scores representing the potentially confounding baseline variables, ANCOVA revealed that the only difference in outcomes between the two groups at 12 months was that the NL group had significantly more severe drug abuse as rated by the ASI—0.6 (SD = 0.012) for NL group versus 0.3 (SD = 0.0038) for the noNL group ($df = 3{,}496$, $F = 3.92$, $p = 0.048$). Following Bonferroni correction for multiple comparisons, this difference was no longer significant.

Outpatients

Baseline Characteristics. Comparisons of baseline demographic and treatment variables in the outpatient sample are presented in Table 3. Again, there were several demographic differences between the two groups. The NL group ($n = 42$) was slightly younger, less likely to be white, more often service connected for PTSD and had a higher disability rating than the noNL group ($n = 405$). As with the inpatients, the NL group was also more likely to be rated as disabled by another psychiatric disorder to some extent, was significantly less likely to be working at the time of initial evaluation, and made less money.

Again, there were no significant differences between the noNL and NL groups with respect to the combat scale score, although veterans in the NL group had significantly higher Mississippi scale total scores and more intrusive, numbing and avoidance, hyperarousal, and total symptoms. The two groups did not differ significantly in terms of guilt symptoms. The NL group had significantly lower measures of alcohol and drug abuse, although they reported significantly more subjective distress on the BSI.

With regards to previous treatment and symptoms, neuroleptic-treated veterans were significantly more likely to have been hospitalized in a psychiatric facility previously, to have been treated at some time on a specialized inpatient unit for PTSD, and to be taking anxiolytic or antidepressant medication. However, there were no differences in the rate of co-morbid alcohol abuse/dependence, drug abuse/dependence, affective, dissociative, bipolar, adjustment, or sleep disorder. This group was also significantly more likely to report hallucinations and trouble with violent behavior in the 30 days prior to enrollment. However, the veterans in the NL group were no more likely to report having serious thoughts or having attempted suicide in the previous 30 days.

Logistic regression identified significant independent differences between the NL and noNL groups on the number of avoidance and numbing symptoms ($p < 0.023$), ASI alcohol composite at baseline ($p = 0.007$), and whether they were taking antikindling medication

TABLE 3
Baseline Characteristics of Veterans Treated as Outpatients for PTSD

	Never Received ($n = 405$)		*Neuroleptic Exposed* ($n = 42$)		*Analysis*		
Baseline Characteristic	*Mean*	*SD*	*Mean*	*SD*	*T*	*df*	*p*
Age (years)	46.2	8.94	43.6	6.21	2.4273	60.2	0.0182
Legacies combat score	10.73	2.675	11.48	2.53	1.7286	444	ns
Mississippi scale total	123.4	22.07	136.8	15.44	5.0612	58.3	0.0001
% service conn for psych (include PTSD)	31	25	44	32	2.3217	160	0.022
Amount take home pay past 30 days	453.5	801.6	72.3	226.6	7.0568	173.6	0.0001
Ment hlth adm to VA	0.31	0.61	0.98	2.34	1.8403	41.6	0.0729
Clinical Symptoms: PTSD							
Mean SCID intrusion symptoms	1.515	0.48	1.708	0.398	2.5176	444	0.0122
Mean SCID numbing and avoidance sympt	1.464	0.459	1.67	0.318	3.8141	60.4	0.0003
Mean SCID hyperarousal symptoms	1.664	0.436	1.862	0.248	4.49	70.9	0.0001
Mean SCID guilt symptoms	1.092	0.731	0.941	0.655	1.286	444	ns
Mean SCID DSM-IIIR symptoms	1.548	0.39	1.747	0.222	5.0475	70.6	0.0001
Mean all SCID symptoms	1.32	0.489	1.344	0.379	0.3775	56.2	ns
Addiction Severity Index							
ASI alcohol composite	0.123	0.203	0.0347	0.082	5.4254	105	0.0001
ASI drug composite	0.035	0.10	0.006	0.0307	4.2265	160.3	0.0001
ASI employment composite	0.478	0.272	0.605	0.229	2.9159	445	0.0037
ASI psychiatric composite	0.531	0.208	0.667	0.165	4.1137	445	<.0001

(*Continued*)

TABLE 3. (*Continued*)

Baseline Characteristic	*Never Received* ($n = 715$)		*Neuroleptic Exposed* ($n = 67$)		*Analysis*		
	Mean	*SD*	*Mean*	*SD*	*T*	*df*	*p*
Brief Symptom Inventory							
BSI psychoticism	1.984	0.922	2.395	0.872	2.7312	438	0.0066
BSI total	2.06	0.851	2.54	0.640	4.4206	55.6	0.0001
	N	%	*N*	%	χ^2	*df*	*p*
Marital status (married)	209	51.6	20	47.62	0.24	1	ns
Race (white)	313	77.28	25	59.52	6.51	1	0.011
Service connected for PTSD	123	30.37	21	50	6.715	1	0.01
Service conn for psych other then PTSD	15	3.7	5	11.9	5.988	1	0.014
Working now	145	35.8	7	16.67	6.21	1	0.0127
Ever hosp for psychiatric diagnosis	242	59.75	35	83.33	28.63	1	<.0001
Taking anxiolytic	89	22	19	45.24	11.239	1	0.001
Taking antidepressant	125	30.86	22	52.36	7.982	1	0.005
Experienced hallucinations-past 30 days	50	12.35	18	42.86	27.466	1	0.001
Trouble violent behavior-past 30 days	158	39.01	28	66.67	11.978	1	0.001
Serious suicide thoughts-past 30 days	114	28.15	14	33.33	0.501	1	ns
Attempted suicide-past 30 days	14	3.46	1	2.38	0.136	1	ns
Trouble reality testing/thought disorder	22	5.45	7	16.67	7.88	1	0.005
Specialized inpatient PTSD program	61	15.06	13	30.95	6.956	1	0.008

($p < 0.023$) or anxiolytic medication ($p = 0.035$), had ever had a psychiatric hospitalization ($p = 0.0023$), or had experienced hallucinations in the past 30 days ($p = 0.0001$).

Outcomes

At 12 months the NL group showed no significant changes on measures of PTSD symptoms (Mississippi total score); number of psychiatric symptoms, alcohol or drug abuse, or employment (as measured by the ASI); or overall subjective distress as well as distress due to psychotic symptoms (as measured by the BSI). The noNL group demonstrated significant improvement only in alcohol and drug use. Adjusting for the propensity scores representing the potentially confounding baseline variables, there were no significant differences between the NL and noNL groups at 12 months.

DISCUSSION

The data presented in this study of 831 inpatients and 554 outpatients with PTSD followed for a year suggest that at baseline there are important clinical differences between those patients prescribed neuroleptics and those not receiving this medication. Approximately 9% of inpatients and 10% of outpatients were treated with neuroleptics, and patients who received these medications had both more psychiatric and more social impairment in both samples. The neuroleptic treated group had more severe PTSD and specifically intrusive symptoms, despite having similar combat exposure. They were more likely to be prescribed other psychiatric medications and to have had a psychiatric hospitalization. They were also less likely to be employed. The use of neuroleptics was not associated with any differences in 12-month outcomes when compared with the group not exposed to neuroleptics.

A small but statistically significant worsening of PTSD symptoms as measured by the Mississippi scale total score was observed in the noNL inpatient group. This is consistent with other analyses of these data (17) and may be due to several factors including stabilization in emergency rooms and general psychiatric units prior to admission to inpatient PTSD treatment along with symptomatic worsening when discharged to outpatient treatment. The overall lack of improvement in both the NL and noNL groups bears further consideration. These data support previous descriptions (23) of the disability and chronic nature of the symptomatology for many veterans seeking treatment for

combat-related PTSD. The types of treatment offered within the VA to patients with combat-related PTSD has also come under scrutiny (24,25).

This study has several limitations. First, the relatively small sample size for the group receiving neuroleptics limits the power to detect statistically significant differences between the two groups. However, some differences were detected suggesting that this sample had ample power to detect robust findings.

Second, the information on neuroleptic exposure does not address the type of neuroleptic used, duration, or dosages. This is not as great a problem as it might first appear in terms of evaluating the effectiveness of neuroleptic treatment of PTSD. As this was "real world" treatment, clinicians used their best judgment about the effectiveness of the pharmacotherapeutic regimen, including neuroleptics. This would lead to the continuation of treatments perceived as successful and termination of those which are not. Thus, while the duration and dosages of neuroleptic treatment are not specified, the identification of all patients who received a trial of neuroleptics during the year should allow for evaluation of the effectiveness of these agents in standard practice.

Since this study was conducted at a time (1990–1994) prior to the ready availability of atypical antipsychotic medications (e.g. clozapine, risperidone, olanzapine, and quetiapine), the applicability of these findings to these medications is unclear. However, no trials have been performed comparing atypical and typical neuroleptics in the treatment of combat-related PTSD, while most comparisons of these two classes of medications in the treatment of schizophrenia have demonstrated only modest differences in symptomatic relief. Additionally, conventional neuroleptics continue to be prescribed for PTSD. We have determined that over a two month period (October and November of 1998) within the PTSD Program at our facility, 26% (129/504) of patients had a neuroleptic prescribed—within that group 54% (70/129) were typical neuroleptics and 46% (59/129) atypical. Finally, this study also reports treatment solely of veterans with combat-related PTSD treated in the VA system. It is unclear how applicable these findings might be in populations with PTSD from non-military trauma.

This study also raises an important methodological issue. In demonstrating no significant improvement associated with the use of neuroleptics in this patient population, this report could be characterized as a "negative study." Reports of these kinds of studies may be particularly important as it has been observed that "negative studies" are typically under-reported in the research literature, leading to a positive-outcome

bias (26) that could mislead readers as to the actual state of knowledge in the field.

CONCLUSIONS

This study represents the first attempt that we are aware of to determine patient characteristics associated with neuroleptic use in the treatment of combat-related PTSD. In centers throughout the VA chosen for their expertise in treating combat-related PTSD, the use of neuroleptics was associated with more severe PTSD and little substantive improvement. In both inpatients and outpatients there were no significant improvements in PTSD symptoms at 12 months.

Our study fails to demonstrate any specific effectiveness of neuroleptics in the treatment of PTSD. With potential side effects such as tardive dyskinesia and little evidence for their effectiveness in this disorder, the use of typical neuroleptics in PTSD is not currently supported by these data. While the newer, atypical neuroleptics possess more favorable risk/benefit ratios in schizophrenia, little information about their role in the treatment of PTSD is available. Because of the limitations of this study, a rigorous evaluation of atypical neuroleptics using an experimental design is needed to determine whether these medications are efficacious in the treatment of severe, refractory, combat-related PTSD.

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